

§1895.01(D), restriction practice under 35 U.S.C. §121, as it applies to national applications submitted under 35 U.S.C. §111(a), is not applicable to a national stage application such as this one. Applicants respectfully point out the PCT administrative instructions in MPEP, Annex B, Part 1, which provide direction on restriction practice under the PCT rules. The Office has not made out a proper case of restriction under the PCT rules, and the Election of Species Requirement should be withdrawn.

Applicants respectfully submit that the above-identified application is now in condition for examination on the merits, and early notice of such action is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,  
MAIER & NEUSTADT, P.C.

  
Norman F. Oblon  
Attorney of Record  
Registration No.: 24,618

Vincent K. Shier, Ph.D.  
Registration No.: P-50,552

Tel: (703) 413-3000  
Fax.: (703) 413-2220  
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Docket No.: **10648-0001-0 PCT**

Serial No: **09/446,109**

**IN THE SPECIFICATION**

Pages 37 and 41-42, please replace Tables 4 and 6 as shown on the attached pages:

**Table 4**  
**Receptor-Binding Affinities<sup>a</sup> and Antagonist Activities<sup>b</sup> in Human PMNs**

Compound	Receptor Affinity <sup>a</sup>		Antagonist Potency <sup>b</sup>		Agonist Activity <sup>c</sup>
	IC <sub>50</sub> (μM)	IC <sub>50</sub> (μM)	IC <sub>50</sub> (μM)	IC <sub>50</sub> (μM)	
<b>SEQ. ID NO: 7</b>	MeFKP (dCh <sub>a</sub> ) [Wr] WR	1.8 (15)	0.085 (9)	No	No
<b>SEQ. ID NO: 8</b>	MeFKP (dCh <sub>a</sub> ) [Wr] WR-	14 (5)	0.5 (3)	No	No
CONH <sub>2</sub>					
<b>SEQ. ID NO: 9</b>	MeFKP (dCh <sub>a</sub> ) WR	11 (5)	0.7 (3)	No	No
<b>SEQ. ID NO: 10</b>	MeFKPLWR	14.4 (1)	>1000 (3)	nd	nd
<b>SEQ. ID NO: 11</b>	AC-F-[KP (dCh <sub>a</sub> ) [Wr] WR]	3.2 (40)	0.090 (5)	No	No
<b>SEQ. ID NO: 12</b>	AC-F-[OP (dCh <sub>a</sub> ) [Wr] WR]	0.28 (6)	0.012 (4)	No	No
<b>SEQ. ID NO: 4</b>	YSFKPMPLaR	6.0 <sup>d</sup>	-	Yes	-
<b>SEQ. ID NO: 1</b>	C5a65-74, ISHKDMQLGR	>1000 <sup>e</sup>	-	-	-
C5a	0.0008 (9)	-	-	Yes	

Number of experiments in parenthesis. Corrected for amino acid content  
 Square brackets indicate cyclic portion.

nd= not determined

<sup>a</sup> 50% reduction in binding of [<sup>125</sup>I]-C5a to intact human PMNs

<sup>b</sup> 50% reduction in myeloperoxidase secretion from human PMNs mediated by 100 nM C5a

<sup>c</sup> Agonist activity in dose range 0.1 nM-1 nM

<sup>d</sup> Finch *et al.*, 1997; <sup>e</sup> Kawai *et al.*, 1991

**--Table 6**  
**Effect of Cyclisation on Antagonist Binding Affinity and Antagonist Potency**

	PEPTIDE	pD <sub>2</sub> ± SE <sup>a</sup>	IC <sub>50</sub> (μM) <sup>a</sup>	(n)	pD <sub>2</sub> ± SE <sup>a</sup>	IC <sub>50</sub> (μM) <sup>b</sup>	(n)
<b>SEQ. ID NO:11</b>	AcF-[KPdChaWR]	5.49 ± 0.22	3.2	4	7.07 ± 0.29	0.09	5
<b>SEQ. ID NO:[18]</b>	AcF-[OPdChaWR]	6.44 ± 0.14*	0.4	9	7.30 ± 0.09	0.05	9
<b>12</b>							
<b>SEQ. ID NO:19</b>	[FWPdChaWR]	4.37 ± 0.36*	43	3	nd		
<b>SEQ. ID NO:20</b>	AcF-[KMcChaWR]	4.81 ± 0.06	15	2	nd		
<b>SEQ. ID NO:21</b>	AcF-[KKdChaWR]	3.94 ± 0.4	116	3	4.88	13	1
Effect of length of linker in cycle on antagonist binding affinity and antagonist potency							
<b>SEQ ID NO:22</b>	AcF-[XPdChaWR]	5.02 ± 0.07	9.5	3	4.71 ± 0.23	20	3
<b>SEQ ID NO:23</b>	AcF-[X <sup>2</sup> PdChaWR]	4.77 ± 0.14*	17	3	6.09 ± 0.08*	0.8	4
<b>SEQ ID NO:[11] 12</b>	AcF-[OPdChaWR]	4.60 ± 0.06*	16	4	6.42 ± 0.10	0.4	4
<b>SEQ ID NO:24</b>	AcKF-[OPdChaWR]	4.96 ± 0.03	11	3	6.73	0.2	1

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Table 6 (cont.)

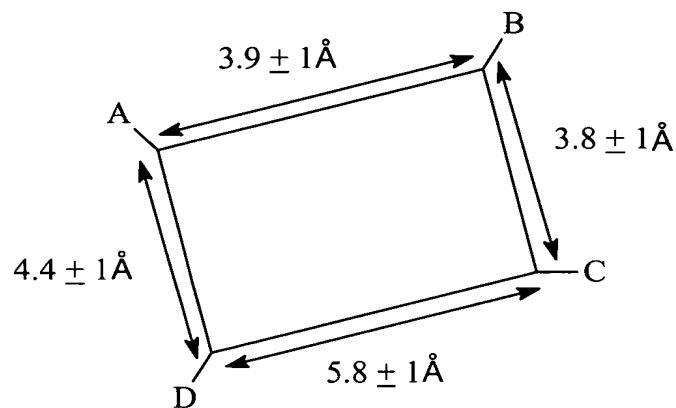
	PEPTIDE	pD <sub>2</sub> ± SE <sup>a</sup>	IC <sub>50</sub> (μM) <sup>a</sup>	(n)	pD <sub>2</sub> ± SE <sup>b</sup>	IC <sub>50</sub> (μM) <sup>b</sup>	(n)
<b>SEQ. ID NO:14</b>	F-[XPdChawR]	4.39 ± 0.10*	41	3	nd		
<b>SEQ. ID NO:16</b>	F-[X <sup>2</sup> PdChawR]	5.42 ± 0.05	3.8	3	6.70 ± 0.04	0.4	3
<b>SEQ. ID NO:25</b>	F-[OPdChawR]	5.51 ± 0.07	3.1	3	5.79 ± 0.34*	1.6	3
<b>SEQ. ID NO:26</b>	F-[KPdChawR]	5.09 ± 0.08	8.1	3	5.55 ± 0.57*	2.8	3
Effect of L-Arg on antagonist binding affinity and antagonist potency							
<b>SEQ. ID NO:17</b>	AcF-[OPdChawR]	6.57 ± 0.05*	0.3	3	7.91 ± 0.17*	0.01	3
<b>SEQ. ID NO:13</b>	F-[XPdChawR]	4.98 ± 0.05	10	3	5.63 ± 0.13*	2.4	3
<b>SEQ. ID NO:15</b>	F-[X <sup>2</sup> PdChawR]	6.50 ± 0.04*	0.3	5	7.36 ± 0.13	0.04	3
<b>SEQ. ID NO:27</b>	F-[OPdChawR]	7.21 ± 0.01*	0.06	3	7.41 ± 0.14	0.04	3
<b>SEQ. ID NO:28</b>	F-[KPdChawR]	6.50 ± 0.12*	0.3	4	6.69 ± 0.04	0.2	3

## IN THE CLAIMS

Please amend Claim 1 as follows:

--1. (Amended) A compound which is an antagonist of a G protein-coupled receptor, which has no agonist activity, and which has a cyclic [on] or constrained acyclic structure adapted to provide a framework of approximate dimensions as set out in Structure I:

Structure I



where the numerals refer to distances between  $C_{\alpha}$  carbons of amino acids or their analogues or derivatives, and A, B, C and D are not necessarily on adjacent amino acids, or analogues or derivatives thereof; and

where the critical amino acid side chains are designated by A, B, C and D, where  
A is any common or uncommon, basic, charged amino acid side chain which serves to position a positively charged group in this position;

B is any common or uncommon, aromatic amino acid side chain which serves to position an aromatic side-chain in this position;

C is any common or uncommon, hydrophobic amino acid side chain which serves to position any alkyl, aromatic or other group in this position;

D is any common or uncommon, aromatic amino acid which serves to position an aromatic side-chain in this position, and has the structure:



where Z is indole, indole methyl, benzyl, benzene, naphthyl, naphthyl methyl, or a derivative thereof; and

R<sup>1</sup> is H or an alkyl, aromatic, acyl or aromatic acyl group.--

